Relationship Between Metabolic Syndrome and Prostate Cancer

Metabolik Sendrom ve Prostat Kanseri Arasındaki İlişki

Metabolic Syndrome and Prostate Cancer

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This study s abstract is presented in EAU 10th South Eastern European Meeting as an oral presentation.

Özet

Amaç: Metabolik sendrom, kanser türleriyle birlikteliği sık tartışılan ve güncel işlenen konulardandır. Bugüne kadar metabolik sendrom ile prostat kanseri arasındaki ilişki, yetersiz çalışma nedeniyle net ortaya konulamamıştır. Biz burada prostat kanseri tanısı konulan hastalarda metabolik sendrom sıklığını ve metabolik sendromun prostat kanserinin diğer parametreleriyle ilişkisi olup olmadığını araştırdık. Gereç ve Yöntem: Transrektal ultrason (TRUS) kılavuzluğunda prostat biyopsisi sonucu prostat kanseri tanısı konulan 102 hastanın patoloji ve kan biyokimya raporları retrospektif olarak değerlendirildi. Hastalar, metabolik sendrom bulunan ve bulunmayanlar olarak 2 gruba ayrılarak, serum PSA seviyeleri, yaşları, total prostat volümleri ve gleason skorları karşılaştırıldı. Bulgular: Çalışmaya dahil edilen toplam 102 prostat kanser tanılı hastanın 18 (%17.6) tanesinde metabolik sendrom tespit edildi. Prostat kanseri bulunan hastalarda metabolik sendromu bulunanların , metabolik sendromu bulunmayanlara göre PSA seviyeleri daha düşükken(p=0.04), prostat volumu ve gleason skorlarında fark bulunamamıştır(p > 0.05) Tartışma: Metabolik sendromlu prostat kanseri hastalarında serum PSA seviyeleri daha düşük bulunmuştur. Bu sonuç metabolik sendromlu hastalarda prostat biopsinin daha düşük PSA seviyelerinde alınmasının gerekip gerekmediği sorusunu akıllara getirmektedir. Bulgularımızı desteklemek için daha fazla hastayla yapılacak, prospektif çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler

İnsulin Direnci; Metabolik Sendrom X; Prostat Kanseri; Prostat Spesifik Antijen; Transrektal Ultrason

Abstract

Aim: Metabolic syndrome has gained increased attention in the last century after researchers identified its important role in cardiovascular mortality and morbidity in developed countries. Despite limited research into the relationship between metabolic syndrome and prostate cancer (PCa), the precise relationship has not been elucidated due to lack of research into the specific factors associated with PCa. To fill this research gap, we evaluated the incidence of PCa in patients with metabolic syndrome and the relationship between metabolic syndrome and the parameters of PCa. Material and Method: We retrospectively evaluated the biochemical analyses of the serum parameters and pathological reports of 102 PCa patients diagnosed by transrectal ultrasound. After determining the incidence of metabolic syndrome in patients with PCa, we divided the patients into two groups, those with and without a diagnosis of metabolic syndrome. We then compared the serum PSA level, age, total prostate volume, Gleason score, triglyceride (TG) level, high-density lipoprotein cholesterol level (HDL-C), blood pressure, and fasting glucose level of the two groups. Results: We included 102 patients with a diagnosis of prostate cancer in the present study. Among the 102 patients, 18 (17.6%) were diagnosed with metabolic syndrome. While the PSA levels of the PCa patients were found to be significantly lower in those with metabolic syndrome compared to those without metabolic syndrome (P=0.04), no difference was found between the groups regarding the other components of PCa (P>0.05). Discussion: Serum PSA level was found to be significantly lower in those with metabolic syndrome. This result leads us to consider whether prostate biopsy should be performed in patients with metabolic syndrome who have lower PSA levels than the levels currently specified for biopsy. Further research into the parameters of PCa needs to be conducted to confirm our findings.

Keywords

Insulin Resistance; Metabolic Syndrome X; Prostate Cancer; Prostate Specific Antigen; Transrectal Ultrasound

DOI: 10.4328/JCAM.4445 Received: 29.02.2016 Accepted: 16.03.2016 Printed: 01.07.2016 J Clin Anal Med 2016;7(4): 520-3
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Introduction

Metabolic syndrome has gained increased attention in the last century after researchers identified its important role in cardiovascular mortality and morbidity in developed countries. According to the criteria of the Third National Health and Nutrition Examination Survey (NHANES III), metabolic syndrome affects 47 million people in the United States or 24% of the general population [1], 44% of whom are 50 years and older [2]. Diagnosis of metabolic syndrome is based on criteria defined by the American National Cholesterol Training Programme Third Adult Treatment Panel (NCEP-ATP III), the International Diabetes Foundation (IDF), and the World Health Organization (WHO) [4-6]. Much evidence indicates that metabolic syndrome is related to various urologic pathologies, such as male infertility [9], nephrolithiasis [21], erectile dysfunction [23], and benign prostate hyperplasia [22]. As the precise relationship between prostate cancer and metabolic syndrome is currently unclear, it continues to be examined.

According to the American Cancer Society, approximately 240,000 men were diagnosed with new prostate cancer (PCa) in 2012 [7]. It is predicted that PCa will be identified as the third most frequent cause of cancer deaths in Europe in 2015 [3]. Since the procedures for prostate biopsy under the guidance of transrectal ultrasound (TRUS) were described by Hodge et al. in 1989, this method has become the gold standard for diagnosis of PCa [8,24]. As a result of the increasing frequency of prostate specific antigen (PSA) scanning and prostate biopsy and recent developments in treatment, the current relative survival ratio is continuously increasing [10].

The literature describes a relationship between PCa and the factors of obesity, abdominal fat distribution, hyperinsulinemia, and hypercholesterolemia, all of which are among the components of metabolic syndrome. However, very few studies have examined the relationship between metabolic syndrome and PCa including all the parameters of metabolic syndrome. As the incidence of both PCa and metabolic syndrome increase with age, examination of this relationship is important. To fill this research gap, we examined the frequency of metabolic syndrome in PCa patients and the relationship between the components of metabolic syndrome and PCa.

Material and Method

Approval of the local ethical committee of Antalya Training and Research Hospital was obtained before initiation of this study. The pathology and blood biochemistry report data of 263 patients who had been diagnosed with PCa and who had undergone prostate biopsy under the guidance of TRUS at Antalya Training and Research Hospital Department of Urology between January 2010 and June 2013 were retrospectively assessed. The diagnosis had been based on findings of a high PSA level (>4 ng/ml) and/or by rectal examination. After lidocaine gel (Cathejell) had been applied as a local anesthetic by the rectal route, periprostatic nerve block was used in the lateral decubitus position under the guidance of TRUS. Using an 18 gauge 30 cm automatic biopsy needle, 10 and 12 core biopsy samples were taken, placed in separately numbered bottles containing 10% formol, and sent to the pathology clinic for examination.

Diagnosis of Metabolic Syndrome

During the histological examination, the biochemistry reports of patients with defined adenocarcinoma were inspected to determine whether they met at least three of the NCEP-ATP III criteria for metabolic syndrome diagnosis regarding serum triglyceride (TG) level, high-density lipoprotein cholesterol (HDL-C) level, fasting blood glucose level, and blood pressure, which are shown in Table 1 (5). 102 of the 263 PCa patients' data was suitable for the study. 102 PCa patients were then divided into two groups based on the findings, a group with metabolic syndrome (18 patients) and a group without metabolic syndrome (84 patients) for comparison of age, serum PSA level, prostate volume, Gleason score, serum fasting blood glucose level, serum TG level, and serum HDL-C level. Patients with a PSA level>50 ng/mL, were <40 years or >80 years of age, or had not undergone biochemical examination within the time period in which PCa had been diagnosed (between January 2010 and June 2013) were excluded from further study.

Table 1. National Cholesterol Education Program Adult Treatment Panel III Metabolic Syndrome Diagnostic Criteria

Waist circumference as a measure of abdominal obesity*	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglyceride level	≥150 mg/dL
HDL cholesterol level	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose level	≥110 mg/dL

Note: Diagnosis of metabolic syndrome is based on the presence of at least 3 of the factors above.

Statistical evaluation

The results were reported as mean ± SD and differences reaching a $p<0.05$ level of significance were considered statistically significant. The variables examined and compared were patient age, prostate volume, Gleason score, serum PSA level, fasting blood glucose level, serum TG level, and serum HDL-C level. The statistical significance of the data, data distribution, and differences between the group means were determined using the t-test for two independent samples, Mann-Whitney U test, Kolmogorov Smirnov-Z test, and/or Wald-Wolfowitz test, as appropriate. SPSS 21.0 software for Windows (SPSS, Chicago, IL, USA) was used for the statistical analyses.

Results

Metabolic syndrome was identified in 18 (17.6%) of the 102 PCa patients included in the study. The mean age of the patients was 67.62±6.44 years, mean PSA level 11.23±7.76 ng/ml, mean Gleason score 6.62±1.05, mean prostate volume 52.18±9.65, mean TG level 128.45±54.85 mg/dl, mean HDL-C level 44.95±10.20 mg/dl, and mean fasting glucose level 117.70±40.71 mg/dl (Table 2).

The mean age, PSA level, prostate volume, Gleason score, TG level, HDL-C level, and fasting glucose level are shown in Table 3. Among the patients with metabolic syndrome, the mean age

Table 2. Patient characteristics

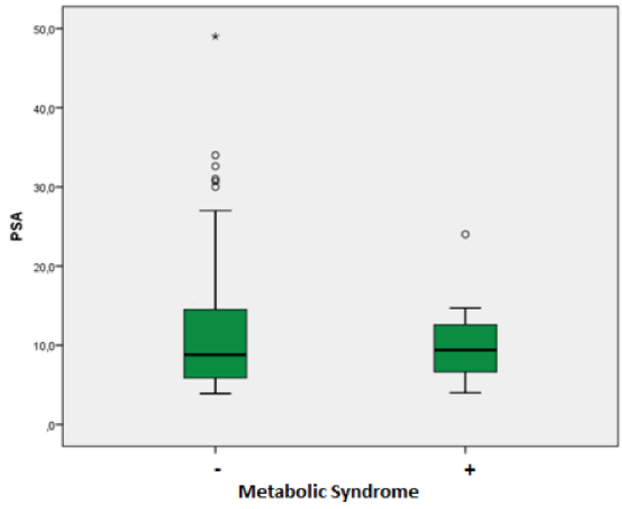
	Age	PSA level	Prostate volume	Gleason score	TG level	HDL-C level	Fasting glucose level
	102	102	102	102	102	102	102
Median±SD	67.62± 6.44	11.23± 7.76	52.18±9.65	6.62±1.05	128.45±54.85	44.95±10.20	117.70±40.71
Minimum	54	3.9	32	6	50	25	71
Maximum	79	49.0	125	10	376	79	325

Table 3. Comparison of prostate cancer patients with and without metabolic syndrome

	Metabolic syndrome (+) (%17.6)	Metabolic syndrome (-) (%82.4)	P
Age	67.78±6.32	67.58±6.50	0.78 (P>0.05)
PSA level	9.96±4.57	11.51±8.28	0.04 (P<0.05)
Prostate level	52.05±9.70	52.10±9.15	0.89 (P>0.05)
Gleasonscore	6.50±0.98	6.64±1.07	0.31 (P>0.05)
TG level	218.08±57.93	109.25±29.32	0.001 (P<0.05)
HDL-C level	33.67±4.33	47.37±9.45	0.013 (P<0.05)
Fasting glucose level	156±51.33	109.49±33.03	0.024 (P<0.05)

was 67.78±6.32, mean PSA level 9.96±4.57 ng/dl, mean prostate volume 52.05±9.70 cc, and mean Gleason score 6.50±0.98. The mean PSA level of the patients with metabolic syndrome was found to be significantly lower than that of the patients without metabolic syndrome (P<0.05) (Figure 1). No statistically significant differences were found between the mean age, Gleason score, or prostate volume of the two groups (P>0.05) (Table 3).

Figure 1. Relationship between metabolic syndrome and prostate specific antigen level



Discussion

The parameters of metabolic syndrome, including insulin resistance, glucose intolerance, hyperlipidemia, and dyslipidemia, have important roles in cardiovascular diseases, especially in the development of coronary artery disease [11]. Nevertheless, the mechanism underlying metabolic syndrome has not been fully elucidated, and conflicting findings have been obtained regarding the relationship between PCa and metabolic syndrome. In a Norwegian study using NCEP-ATP III criteria and following 16,209 men between 40 and 49 years for 27 years, Lund Haheimet et al. observed a greater incidence of PCa in patients who met criteria for metabolic syndrome at a ratio of 56% [12]. In contrast, in a U.S. study of 6,249 patients, Tande et al. observed a lower incidence of PCa in men with metabolic syndrome [13]. Several factors may be responsible for the different results obtained by cohort studies examining the relationship between PCa and metabolic syndrome. Four of these reasons are the use of different sample sizes, the use of follow-up periods of different lengths, the use of different definitions of metabolic syndrome, and the inability to explicitly examine concomitant factors. Moreover, none of the four sets of criteria used in the identification of metabolic syndrome (the World Health Organization, NCEP-ATP III, European Group for the Study of Insulin Resistance, and IDF criteria) is considered a gold standard, and each addresses different aspects of metabolic syndrome. Obtaining of conflicting research findings and the use of differing sets of criteria prevent identification of the precise relationship between PCa and metabolic syndrome.

When researchers examined the components of metabolic syndrome individually, they obtained several conflicting results, although all appear to indicate that obesity is the essential factor in the development of metabolic syndrome. In a study assessing 950,000 Norwegian men, Engeland et al. observed that obese patients between 50 and 59 years have a 58% increased risk of PCa risk compared to patients with a normal BMI [14]. Interestingly, in a study examining the data collected by the USA Health Professionals Follow-Up Study, Giovannucci et al. found that while BMI is significantly negatively correlated with PCa risk in patients between 50 and 59 years, it is slightly positively correlated with PCa risk in patients over 60 years [15]. In an assessment of the data of 18,939 patients collected by the Helsinki Cardiac Study, Tuohimaa et al. determined that BMI over 28kg/m2 and systolic blood pressure over 150 mmHg increased PCa risk two-fold and when low HDL-C level (≤ 1.05 mmol/L) is also present with these factors, the risk increases three-fold [16].

In the study of 2007 men with no PCa, Kim et al. found that metabolic syndrome adversely affected PSA levels [17]. Kristal et al. hypothesized that in patients with metabolic syndrome, low PSA level is related to obesity-related hemodilution and low levels of circulatory androgens [18]. They posited that in obese patients, both a lower PSA level and a larger gland structure can decrease the sensitivity of prostate needle biopsy and can delay diagnosis of cancer. In accordance with this hypothesis, we found that the PSA levels of the PCa patients who we examined were lower in those with metabolic syndrome compared to those without metabolic syndrome.

Several studies have indicated that metabolic syndrome may cause more aggressive PCa. In a wide meta-analysis assessing 112 studies, MacInnis et al. found that a 5 kg/m2 increase in BMI was associated with a 5% increase in the risk of PCa overall, as well as a greater increase in advanced stage disease

(RR 1.12) compared to local stage disease (RR 0.96) [20]. In a retrospective of 1415 patients, Jayachandran et al. observed that radical prostatectomy pathology specimens of patients with BMI ≥35 were associated with worse prognostic findings, specifically those with a Gleason score ≥7, as well as positive surgical limit, extra prostatic distribution, and seminal vesicle invasion [20]. In our study, we found no significant differences in the Gleason scores, as determined from the prostate needle biopsy results, between the patients with metabolic syndrome and the patients without metabolic syndrome.

Among the NCEP-ATP III-2001 criteria, the primary factors that we examined were serum HDL levels, triglyceride levels, and fasting blood glucose levels. Because of the retrospective nature of our study, we were unable to examine several parameters, such as waist circumference and blood pressure. If these parameters had been included, we may have been able to identify a greater number of patients with metabolic syndrome. Of the 102 PCa patients we included according to these three criteria, we identified metabolic syndrome in 18 (17.6%) patients. When we compared several factors of the PCa patients with metabolic syndrome, such as age, serum PSA level, Gleason score, and total prostate volume, with those of the PCa patients without metabolic syndrome, we found that serum PSA level is significantly lower in those with metabolic syndrome. This result leads us to consider whether prostate biopsy should be performed in patients with metabolic syndrome who have lower PSA levels than are currently specified for biopsy. Other than PSA level, we found no significant differences between the two groups regarding age, Gleason score, or total prostate volume.

Conclusions

Although several factors associated with PCa appear to be related to the development of metabolic syndrome, the precise relationship between metabolic syndrome and PCa will remain unclear until all these factors are investigated in detail. As research continues to be conducted into this relationship, prostate biopsy should be performed in patients with metabolic syndrome who have lower PSA levels than are currently specified for biopsy.

Conflict of interest:

The authors declare that they have no conflict of interest.

List of abbreviations:

HDL-C: High-density lipoprotein cholesterol
IDF: International Diabetes Foundation
NCEP-ATP III: Third Report of the National Cholesterol Education Program (NCEP)Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP-III)
NHANES III: Third National Health and Nutrition Examination Survey
Prostate cancer: PCa
Prostate specific antigen: PSA
TG: triglyceride
TRUS: transrectal ultrasound
WHO: World Health Organization

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How to cite this article:

Bas S, Yuksel M, Yılmaz S, Yalcınkaya S, Islamoglu E, Tokgoz H, Ipekci T, Savas M. Relationship Between Metabolic Syndrome and Prostate Cancer. J Clin Anal Med 2016;7(4): 520-3.